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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/025,730	12/18/2001	Y. Tom Tang	PF-0635-2 DIV	8039

27904 7590 05/11/2004

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/025,730	TANG ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,11,12 and 58-72* is/are pending in the application.

4a) Of the above claim(s) *1-3,12,60,62,71 and 72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11, 58-59, 61, 63-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-3, 11-12, 58-72 are pending.

2. Applicant's election with traverse of Group IV, claim 11 (now claims 11, 58-59, 61 and 63-70) drawn to an antibody which specifically binds to a polypeptide comprising amino acid of SEQ ID NO: 1, filed on 3/24/04, is acknowledged.

Applicant's traversal is on the grounds that method of using the antibodies of Groups IV should be examined together with the claims of Group IV. Applicant submits that it would not be an undue burden on the Examiner to examine method of using the antibody because the searches for the claimed antibodies and these new method claims would substantially overlap. This is not found persuasive because the antibody of Group IV and the method of using the antibody of Group IV (new claims 60, 62, 71 and 72) are related as product and process of using. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antibody of Group IV can be used for affinity purification, in addition to the methods of diagnosing and detecting recited. Therefore the methods of diagnosing and the method of detecting using the antibody of Group IV are distinct and independent, and searches of all groups would place an undue burden upon the examiner due to the distinct and divergent subject matter of each Group. Further, a prior art search also requires a literature search. It is an undue burden for the examiner to search more than one invention.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 1-3, 12, 60, 62, 71 and 72 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 11, , 58-59, 61 and 63-70 are under examination as they read on an antibody which specifically binds to a polypeptide compring amino acid of SEQ ID NO: 1, fragments and composition thereof.

5. The U.S. Patent 6,365,371 and 6,071,721 cited on the PTO FORM 892 is issued from the parental application serial No. 09/470,253 and 09/190,965, respectively and will not be supplied.

6. Claims 11, 58-59, 61 and 63-70 are objected to because they are dependent on a non-elected claim 1 and should be written as an independent claim.

7. The oath or declaration filed 8/26/02 is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because inventor Neil C. Corley Residence and P.O Address have been altered without being initialed and dated.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 61 and 63-68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The term "specificity" recited in claims 63 and 66, line 1 is ambiguous and unclear and the metes and bounds of the claimed "specificity" is not defined. It is well known in the art that every antiserum has a different specificity because the repertoire of antibodies produced by animal is somewhat different. Thus, it is unclear one skill in the art would be able to make an antibody with the specificity of the antibody to SEQ ID NO:1.

B. Claim 61 has no antecedent basis in base claim 59, because claim 59 recites a composition comprising an antibody per se, whereas a labeled antibody is recited in claim 61.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 11, 58-59, 61 and 63-70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody which specifically binds to a polypeptide of SEQ ID NO:1, does not reasonably provide enablement for any antibody which specifically binds to any polypeptide **comprising a naturally occurring amino acid sequence at least 90%** identical to an amino acid sequence of SEQ ID NO: 1 in non-elected claim 1(b); or any antibody which specifically binds to **any biologically active fragment** or any **immunogenic fragment** of a polypeptide of SEQ ID NO:1 in non-elected claim 1(c-d); or a method of preparing making a polyclonal/monoclonal antibody with the **specificity** of the antibody of the embodiment of claim 11 comprising immunizing an animal with a polypeptide consisting of **any immunogenic fragment** in claims 63 and 66. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

There is insufficient guidance and direction as to how to make the claimed antibodies, wherein the antibodies which specifically binds to any polypeptide comprising an amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:1; or any antibody against any biologically active fragment or any immunogenic fragment of a polypeptide of SEQ ID NO:1.

The present specification fails to provide sufficient disclosure of fragments of SEQ ID NO:1 immunogenic or biologically active, or a polypeptide at least 90% sequence identity to the sequence of SEQ ID NO:1 which include numerous changes and variation. The specification does not provide sufficient guidance as to which of the amino acids may be changed while the calcium binding activity is retained. In addition, the term "comprising" in non-elected claim 1b is open-ended, it expand the "naturally occurring polypeptide" to include additional non disclosed amino acids on either or both sides of the N-terminal or C-terminal of the at least 90% identical polypeptide of SEQ ID NO:1. Further, the specification fails to provide guidance on how to measure and determine the antibody "specificity", and further to make or prepare an antibody that would have that same "specificity".

The one of the uses of the claimed polypeptide is to make antibody then any change in the polypeptide of SEQ ID NO: 1 would affect the binding specificity of the antibody. Colman *et al* in Research in Immunology (145(1):33-36, 1994) teach single amino acid changes in an antigen can effectively abolish antibody antigen binding. Further, Lederman *et al* in Molecular Immunology (28:1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document).

Because of the unpredictability and the lack of guidance, an undue experimentation would be required to determine which modifications would be acceptable to retain occluding structural and functional activity, and the fact that the relationship between the sequence of a protein/peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g. see Ngo *et al* in the Protein Folding problem and Tertiary Structure prediction, 1994, Merz *et al.*, (ed), Birkhauser, Boston, MA, pp.433 and 492-495), it would require an undue amount of experimentation for one of skill in the art to arrive at *biologically active* or *immunogenic fragments* or *a naturally occurring amino acid sequence at 90% identical to an amino acid sequence of SEQ ID NO:1* encompassed by the claimed invention.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

12. Claims 11, 58-59, 61 and 63-70 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of enabling for an antibody which specifically binds to a polypeptide of SEQ ID NO:1.

Applicant is not in possession of any antibody which specifically binds to any polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid

sequence of SEQ ID NO: 1 in non-elected claim 1(b); or any antibody which specifically binds to any biologically active fragment or any immunogenic fragment of a polypeptide of SEQ ID NO:1 in non-elected claim 1(c-d); or a method of preparing making a polyclonal/monoclonal antibody with the specificity of the antibody of the embodiment of claim 11 comprising immunizing an animal with a polypeptide consisting of any immunogenic fragment in claims 63 and 66.

Applicant has disclosed only amino acid of SEQ ID NO: 1; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

As for the recitation of "naturally-occurring polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1", the court said that all of the claims of a patent were invalid because the specification did not provide an adequate written description of the rat DNA that was required by the asserted claims. The court said that " an adequate written description of a DNA ... 'requires a precise definition, such as by structure, formula, chemical name, or physical properties.' Not a mere wish or plan for obtaining the claimed chemical invention." *Eli Lilly*, 119 F.3d at 1566 (quoting *Fiers*, 984 F.2d at 1171). Likewise, Applicant fails to satisfy the written-description requirement where the claimed invention called for a "naturally-occurring polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1" and "a polypeptide having an immunogenic fragment", but did not disclose such "variants" and "fragments". The court stated that "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it, what is required is a description of the DNA itself." *Fiers* 984 F.2d at 1170.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 11, 64, 67, 69 and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyamoto *et al* (Mol Reprod Dev. 34(1):1-7, 1993) in view of Alisa Campbell (General properties and applications of monoclonal antibodies, Elsevier Science Publishers, 1984, section 1.1), as is evidanced by Bost *et al.* (Immunol. Invest. 1988; 17:577-586).

Miyamoto *et al* teach a mouse Ca2+ binding protein (CBP), MO25, comprising a 341 amino acids , which has 81% identity to claimed SEQ ID NO: 1. (see attached sequence alignment in particular). The referenced protein of the MO25 comprising several fragments that has consecutive amino acids that are 100% identical to fragments of claimed polypeptide of SEQ ID NO: 1.

The claimed invention differs from the reference teachings only by the recitation of an isolated antibody of claim 11 which specifically binds to a polypeptide comprising an amino acid sequence of SEQ ID NO:1 in claims 1(a), a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 1 in claim 1(b).

Campbell teaches that it is customary now for any group working on a macromolecule to both clone the genes coding for it and make monoclonal antibodies to it (see page 3 figure 11.1 in particular). One field of research in which monoclonal antibodies may prove of particular value is in the study of chromosomal proteins. The search for those chromosomal proteins which are responsible for determining cell phenotype has been particularly long and comparatively fruitless and monoclonal antibodies are ideal tools for the dissection of the complex mixture of proteins. As hybridoma production becomes a more routine laboratory technique (see page 29 and 30 under Basic research in particular).

Further, antibodies "cross-react" with antigens with homolgous amino acid residues. Although Miyamoto *et al* does not teach specific amino acid sequence of SEQ ID NO:1, binding to "SEQ ID NO:1" is considered an inherent property of the reference antibody. As is evidenced by Bost *et al* that an antibody "cross-reacts", i.e. binds to more than one protein sequence, which mean that "specifically bind" with both proteins. Bost *et al* (Immuno. Invest. 1988 ;17:577-586) describe antibodies which "cross-react" with IL-2 and HIV envelope protein, but establish that the binding of each protein is due to the presence of a homologous sequence in each protein in which 4-6 residues were identical (see entire document, especially the Abstract and Discussion).

Claims 64, 69 and 70 are included because an antibody is the same antibody irrespective of how it is made.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to to make a monoclonal antibody as taught by Campbell against the calcium binding protein taught by the Miyamoto *et al.*

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because it was customary at the time the invention was made to make monoclonals against any new macromolecule as taught by Campbell for the search for those chromosomal proteins which are responsible for determining cell phenotype and because the monoclonal antibodies are ideal tools for the dissection of the complex mixture of proteins.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. Claims 63 and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyamoto *et al* (Mol Reprod Dev. 34(1):1-7, 1993) in view of Alisa Campbell (General properties and applications of monoclonal antibodies, Elsevier Science Publishers, 1984, section 1.1), as is evidanced by Bost *et al.* (Immunol. Invest. 1988; 17:577-586), as applied to claims 11, 64, 67, 69 and 70 above, and further in view of Harlow (1989).

The teachings of the Miyamoto *et al* reference, Campbell reference and Bost et al have been discussed, supra.

The claimed invention differs from the reference teaching only by the recitation of a method of preparing a polyclonal antibody in claim 63 and a method of making monoclonal antibody in claim 66.

Harlow *et al* teach a method of producing polyclonal antibody to any antigen (see entire document and page 96, in particular). Harlow *et al* further teach that for practical reasons,

rabbits represent a good choice for the routine production of polyclonal sera since they are easy to keep and handle and antibody produced are well characterized and easily purified. Further, Harlow et al teach a method of producing monoclonal antibodies comprising immunizing an animal (i.e. a mouse) with a protein or portion thereof (i.e. fragments), harvesting spleen cells from said animal, fusing said spleen cells with myeloma cell line, and culturing said fused cells (i.e hybridoma) under conditions that allow production of said antibody. Harlow et al further teach that the monoclonal antibodies stems from their specificity, homogeneity and ability to be produced in unlimited quantities (see pages 141-157 in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to produce polyclonal or monoclonal antibody using the method taught by Harlow *et al* with the calcium binding protein taught by Miyamoto *et al.*

One ordinary skill in the art at the time the invention was made would have been motivated to make polyclonal antibody to calcium binding because Harlow *et al* teach rabbits represent a good choice for the routine production of polyclonal sera since they are easy to keep and handle and antibody produced are well characterized and easily purified. Harlow *et al* further the monoclonal antibodies produced exhibit a high degree of specificity and great affinity.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

16. Claim 58 is rejected under 35 U.S.C. 103(a) as being unpatentable over Miyamoto *et al*, in view of Alisa Campbell, as is evidanced by Bost *et al*, as applied to claims 11, 64, 67, 69 and 70 above, and further in view of Owens *et al* (1994).

The teachings of the Miyamoto *et al* reference, Campbell reference and Bost et al have been discussed, supra.

The claimed invention differs from the reference teaching only by the recitation of a chimeric antibody, a single chain antibody, a Fab fragment, a $F(ab')_2$ fragment or a humanized antibody.

Owens *et al* teach the modification of murine antibodies such as a chimeric antibody, a single chain antibody, a Fab fragment, a $F(ab')_2$ fragment or a humanized antibody antibodies monoclonal antibody technology, chimeric, single chain, Fab fragments, and $F(ab')_2$. Owens *et al* further teach humanized antibodies use in therapy of human diseases or disorders, since the human or humanized antibodies are much less likely to induce an immune response. Also, antibody fragments are the reagents of choice for some clinical applications, and the chimeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement – dependent cytotoxcity (see the entire document).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to make a monoclonal/polyclonal antibody as taught by Campbell or Harlow against the calcium binding protein taught by the Miyamoto *et al* and produce the antibody as a chimeric, a humanized antibody, a Fab, a $F(ab')_2$ fragments or a single chain antibody taught by the Owens *et al.*

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the humanized antibodies are much less likely to induce an immune response and because the antibody fragments are the reagents of choice for some clinical applications and the chimaeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement-dependent cytotoxcity as taught by Owens *et al.*

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

17. Claim 59, 61, 65 and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyamoto *et al* in view of Alisa Campbell, as is evidanced by Bost *et al.*, as applied to claims 11, 64, 67, 69 and 70 above, and further in view of U.S. Patent No. 6,210,675.

The teachings of Miyamoto *et al*, Campbell and Bost *et al* references, and the `675 patent have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation of a composition comprising an antibody and an acceptable excipients/suitable carrier in claims 59, 65 and 68 and a composition wherein the antibody is labeled in claim 61.

The '675 patent teaches that an antigenic fragment of an antigen having a minimum of five amino acids and each fragment is usually coupled to some carrier molecule to facilitate the induction of an immune response (column 2, lines 41-65 and column 3, lines 1-5 in particular). Furthermore, the '675 patent teaches antibodies and methods of producing polyclonal and monoclonal antibodies to a polypeptide (column 5, lines 5-47). Polyclonal antibodies against a polypeptide can be obtained by injecting a polypeptide, into a mammalian host such as a mouse, rat, sheep or rabbit and recovering the antibody thus produced; plasma samples being taken at appropriate intervals are assay for the antibody specificity. Monoclonal antibodies against a polypeptide can be obtained by fusing cells of an immortalizing cell line with cells which produce antibody against the polypeptide, and culturing the fused immortalized cell line. Also, the '675 patent teaches that antibodies produced can be used in quality control testing of the polypeptide; purification of the polypeptide or lysate; epitope mapping, when labeled, as a conjugate in a competitive type assay; and for antibody detection (column 5, lines 6-13 in

particular). Finally, the '675 patent teaches that the antibody is in solution (column 7, lines 58-62 in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to formulate the antibody in a composition and to link the antibody to a label as taught by `675 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the composition antibodies produced can be used in quality control testing of the polypeptide; purification of the polypeptide or lysate; epitope mapping, when labeled, as a conjugate in a competitive type assay; and for antibody detection as taught by '675 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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April 30, 2004

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